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SYSTEM AND METHOD FOR THERAPY AND DIAGNOSIS COMPRISING TRANSLATORY DISTRIBUTOR FOR DISTRIBUTION OF RADIATION

Field of the Invention

The invention relates generally to a system and a method for therapy and diagnosis in a mammal. More particularly, the system and method relate to a system and method for tumour therapy and diagnosis in a mammal. Even more particularly, the invention relates to a system and method for photodynamic therapy (PDT) and/or photothermal therapy (PTT) and/or diagnosis (PDD) of a site on and/or in a body, wherein radiation is conducted to the site for reaction with the radiation, wherein the system comprises a distributor of radiation from at least one source of radiation to a reaction site, and from the reaction site to at least one radiation sensor, respectively, and wherein the reaction site preferably is a tumour site with a tumour, such as a malignant tumour.

Background of the Invention

Within the field of medical therapy of tumour diseases, a plurality of treatment modalities has been developed for the treatment of malignant tumour diseases: operation, cytostatic treatment, treatment with ionising radiation (gamma or particle radiation), isotope therapy and brachytherapy employing radioactive needles are examples of common treatment modalities. In spite of great progress within therapy, the tumour diseases continue to account for much human suffering, and are responsible for a high percentage of deaths in Western countries. A relatively new treatment modality, photodynamic therapy, commonly abbreviated PDT, provides an interesting

complement or alternative in the treatment field. A tumour-seeking agent, normally referred to as a precursor or sensitizer , is administered to the body intravenously, orally or topically. It accumulates in malignant tumours to a higher extent than in the surrounding healthy tissue. The tumour area is then irradiated with non-thermal red light, normally from a laser, leading to excitation of the sensitizer to a more energetic state. Through energy transfer from the activated sensitizer to the oxygen molecules of the tissue, the oxygen is transferred from its normal triplet state to the excited singlet state. Singlet oxygen is known to be particularly toxic to tissue; cells are eradicated and the tissue goes in necrosis. Because of the localisation of the sensitizer to tumour cells a unique selectivity is obtained, where surrounding healthy tissue is spared. The clinical experiences, using in particular haematoporphyrin derivative (HPD) and delta aminolevulinic acid (ALA) have shown good results.

Sensitizers also exhibit a further useful property; to yield a characteristic red fluorescence signal when the substance is excited with violet or ultraviolet radiation. This signal clearly appears in contrast to the autofluorescence of the tissue and can be used to localise tumours and for quantifying the size of the uptake of the sensitizer in the tissue.

The limited penetration in the tissue of the activating red radiation is a big drawback of PDT. The result is that only tumours less than about 5 mm thickness can be treated by surface irradiation. In order to treat thicker and/or deep-lying tumours, interstitial PDT (IPDT) can be utilised. Here, light-conducting optical fibres are

brought into the tumour using, e.g. a syringe needle, in the lumen of which a fibre has been placed.

In order to achieve an efficient treatment, several fibres have been used to ascertain that all tumour cells are subjected to a sufficient dose of light so that the toxic singlet state is obtained. It has been shown to be achievable to perform dose calculations of the absorptive and scattering properties of the tissue. E.g., in the Swedish patent SE 503 408 an IPDT system is described, where six fibres are used for treatment as well as for measurement of the light flux which reaches a given fibre in the penetration through the tissue from the other fibres. In this way an improved calculation of the correct light dose can be achieved for all parts of the tumour.

According to the disclosure of SE 503 408, the light from a single laser is divided into six different parts using a beamsplitter system comprising a large number of mechanical and optical components. The light is then focused into each of the six individual treatment fibres. One fibre is used as a transmitter while the other fibres are used as receivers of radiation penetrating the tissue. For light measurement light detectors are mechanically swung into the beam path which thus is blocked, and the weak light, which originates from the fibres that collected the light which is administered to the tissue, is measured.

However, such open beam paths result in a strongly lossy beamsplitting and the resulting losses of light drastically impair the light distribution as well as the light measurement. Furthermore, such a system must often be adjusted optically, which is also an important drawback in connection with clinical treatments. The system is also

large and heavy and difficult to integrate into a user-friendly apparatus.

A solution to these problems has been proposed in PCT/SE02/02050, wherein a distributor for radiation having two discs rotating relative each other is described. The radiation distributor couples optical fibres between different modes. For switching between several light sources to one fibre going to the patient, an assembly with a total of four discs is described. There is a need to further reduce the size of the described solution in order to further minimise the size of the system.

Thus, there is a need for a new compact device allowing distributing of radiation in a system for therapy and diagnosis in a mammal, wherein the therapy and diagnosis comprises PDD, PDT and PTT.

Summary of the Invention

The present invention overcomes the above identified deficiencies in the art and solves at least the above identified problems by providing a system and a method according to the appended patent claims, wherein a very practical and efficient implementation of interactive IPDT is achieved in that different optical measurements for diagnostics and dosimetry can be performed in an integrated and simple way. An important application of the invention is interactive, interstitial photodynamic therapy, and/or interactive photothermal tumour therapy. According to the invention, the size of a system using existing radiation distributors, such as described in PCT/SE02/02050 is further reduced. Furthermore, the invention is an alternative solution to the problems and drawbacks associated with the systems according to the prior art.

According to one aspect of the invention, a system for therapy and/or diagnosis comprises at least one radiation distributor, which comprises at least one translatory displacement element, such as a sliding sledge, having preferably at least two parts translatory displaceable relative each other for coupling a plurality of radiation conductors in different constellations. Switching between the different constellations is carried out by displacing at least one translatory element, i.e. by motion of the translatory element along its longitudinal axis relative the other part. Thus operations such as coupling of one radiation source to a single output radiation conductor and/or coupling of a plurality of radiation conductors from a site in a mammal to at least one radiation detector are accomplished in an effective way by means of a system comprising a compact device.

One translatory displacement device element may be fixed and the other movable or both are movable, e.g. with relation to a fixed housing.

Brief Description of the Drawings

In order to explain the invention more detailed, a number of embodiments of the invention will be described below with reference to the appended drawings, wherein

Fig. 1 is a schematic view illustrating an embodiment of the invention in the tumour therapeutic mode, in a system according to the invention, wherein light guides are arranged interstitially inserted in a tumour;

Fig. 2 is a schematic view illustrating another embodiment of the invention in the tumour diagnostic mode;

Fig. 3 is a schematic view of the embodiment according to Fig. 2 in another diagnostic mode;

Fig. 4 is a schematic view illustrating a further embodiment of the system according to the invention with a radiation distributor coupling a radiation detector in diagnostic mode;

Fig. 5 is a schematic view illustrating yet another embodiment of the invention in use of the system according to the invention, with a translatory radiation distributor integrated in a rotatable radiation distributor;

Fig. 6 is a schematic view showing the embodiment of Fig. 5 in a diagnostic mode;

Fig. 7 is a schematic view showing the embodiment of Fig. 5 with discs of the rotatable radiation distributor taken apart;

Fig. 8 is a schematic view illustrating the radiation distributors of Fig. 5 in use, and

Fig. 9 is a planar top view over a translatory radiation distribution element with holes for receiving light guides arranged in said element.

Description of embodiments

Fig. 1 is a schematic view illustrating an embodiment of the invention in a system according to the invention. In order to simplify the description of the embodiments, reference numerals for similar elements shown in the figures are not repeated in all figures. An embodiment 100 of the distributor of the system according to the invention is now described with reference to Figs. 1-4 and Fig. 9. A distributor 1 for radiation comprises two substantially in close proximity to each other lying longitudinal translatory elements made of, e.g. 1 cm thick steel. The longitudinal translatory elements are hereby arranged in such a manner that they may move translatory relative to

each other in such a manner that a plurality of radiation conductors 144-146 or 102a-102f, 131a-131j, 160 respectively, such as optical fibres, being fixed to holes 2 in the first translatory element 110, 150 are coupled to a second plurality of fibres 160 or 120a-120f respectively, being fixed to holes 2 in the second translatory element 111, 151, by appropriately positioning the two elements relative to each other. The system 100 shown in Fig. 1 comprises two such radiation distributors A and B comprising the translatory elements 110, 111, 150, 151. These elements are shown as longitudinal elements in Figs. 1 to 4. However, they may have another geometrical shape, as can be seen in Figs. 5-8. Furthermore, at least one of the elements may be integrated into a housing etc. The elements may be sledges, for coupling either treatment radiation or diagnostic radiation to a patient.

In the diagnostic position radiation is coupled to at least one radiation detector 130. The diagnostic part of system 100 comprises a 2-1, 3-1, ..., n-1 radiation distributor A, wherein n is the number of diagnostic light sources 141, 142, 143. The radiation distributor consists of two translatory displaceable elements 150, 151. Each of the two elements is displaceable with relation to the other translatory element, in such a manner that one diagnostic light source at a time is coupled to radiation conductor 160 and further to the site in the patient to be treated via a second radiation distributor B. This diagnostic mode will be described in more detail below, with reference to Figs. 2 and 3. Furthermore a plurality of diagnostic radiation sources may be used simultaneously. In this case several diagnostic radiation sources may be modulated, so

that the diagnostic radiation may be detected simultaneously by means of e.g. a lock-in method or by multiplexing the signals, wherein the therapeutic radiation preferably is shut off in diagnostic mode.

A main radiation distributor B comprises two translatory elements 110, 111. The two translatory elements 110, 111 are displaceable with relation to the other translatory element, as indicated by the arrows 105, 106. The displacement is controlled in such a manner that a plurality of radiation conductors 120a-120f lead radiation to and from a tumour site in a patient. Main radiation distributor B switches between the diagnostic modes and the therapeutic mode. The radiation conductors 120a-120f leading to and from the patient are fixed to the translatory element 111. The translatory element 110 of the main radiation distributor B comprises a (3N-1) to N radiation distributor, wherein N is the number of radiation conductors 120a-120f to/from the patient fixed in translatory element 111 and (3N-1) is the number of radiation conductors fixed in translatory element 110 of which N are radiation distributors 102a-102f coupled to light sources 101a-101f and 2(N-1) are radiation distributors 131a-131j coupled to radiation detector 130, and one, 160, is coupled to the diagnostic light 240.

In the therapeutic mode, B is adjusted in such a manner, as shown in Fig. 1. Treatment radiation originating from the light sources 101a-101f is coupled to radiation conductors 102a-102f. These radiation conductors, preferably light guides or optical fibres, are coupled to translatory displacement element 110. Element 110 is aligned with translatory displacement element 111 in such a

manner that the light from light sources 101a-101f is coupled to radiation conductors 120a-120f and further to the treatment site in the patient.

In diagnostic mode the radiation distributor A is adjusted such that one of diagnostic light sources 141, 142, 143 is coupled to fibre 160. Alternatively, only one diagnostic light source is used in the system, as shown in Figs. 2 and 3. Main radiation distributor B is in diagnostic mode adjusted such that one of the N patient fibres 120a-120f is coupled to a diagnostic light conducting radiation conductor 160. This is accomplished by transversally sliding the translator elements 110, 111 relative each other, as indicated by arrows 205, 206. The radiation, which is being transmitted back from the site in the patient through the remaining (N-1) fibres from the plurality of fibres 120a-120f, is also called diagnostic radiation. This diagnostic radiation is coupled to (N-1) radiation conductors from a plurality of radiation conductors 131a-131j leading to the radiation detector 130. Subsequently, the radiation distributor B is adjusted in such a way that another of the N patient fibres 120a-120f is coupled to diagnostic light emitting fibre 160. This is accomplished by once again sliding the translator elements 110, 111 transversally relative each other, as indicated by arrows 305, 306. In this way another set of (N-1) fibres is coupled to (N-1) radiation conductors from a plurality of radiation conductors 131a-131j leading to the radiation detector 130. This is repeated N times, until all N coupling combinations of fibre 160 to the N patient fibres, is accomplished. In case a plurality of n diagnostic light sources is present in the system, the N measurements are

carried out with each of the n light sources, which results in (N*n) diagnostic measurements, each measurement delivering (N-1) measurement values. Alternatively to the sequence described above, the n light sources are applied subsequently, before switching to the next input fibre to the patient. The detector may be a single detector or a plurality of detectors or an array detector.

Fig. 4 is a schematic view over another embodiment according to a system of the invention, wherein a further radiation distributor C is used for minimising the number of radiation conductors leading to detector 430. Distributor C comprises two translatory elements 470, 471. The two translatory elements 470, 471 are displaceable with relation to the other translatory element respectively. A plurality of (N-1) radiation conductors 431a-431e, corresponding to the (N-1) radiation conductors conducting diagnostic radiation from the patient, are fixed to the translatory element 470 and lead to the detector 430. 2*(N-1) radiation conductors 131a-131j lead from the translatory element 110 to the translatory element 471. Radiation distributor C is adjusted in such a manner that only the active (N-1) radiation conductors of the plurality of conductors 131a-131j are couple to the detector 430 through radiation conductors 431a-431e. Alternatively, the translatory element 471 may be integrated with the translatory element 110 and the translatory element 470 may be integrated with the translatory element 111 (not shown in the Figs.). In this way, the one and same translator may be used for therapy and diagostic measurements.

N = 6 and n = 3 in the exemplary embodiments given above. However, other numbers of N and n are equally possible.

For calibration purposes of at least the mechanical part of the system according to the present invention, a 7^{th} hole may be present in translator 111. Preferably this hole is located exactly between fibres 120d and 120c on translator 111, with reference to the linear translator shown in Figs. 1-4. Concerning the disc 510 shown in Figs. 5-8, the 7^{th} hole is preferably located anywhere in between holes 513 on the disc 510. The seventh hole is used to exactly define the position of an input fibre in a hole on the opposite element of a radiation distributor. The seventh hole is either directly equipped with a radiation sensor or connected to a radiation sensor for detecting radiation transmitted from a radiation conductor facing the seventh hole from the opposite side. In this way the positioning of the elements of a radiation distributor may be calibrated. For instance the position of the seventh hole may be used to zero the position of stepping motors driving these elements. The seventh hole may equally be used to calibrate the position of translatory element 550 or any other translatory element of the system according to the invention in the same way.

For calibration purposes of the entire system according to the invention, including the radiation part, the overall performance of the system is recorded prior to the treatment by direct measurements on a calibrated tissue phantom made of, e.g., a sterile intralipid-water solution or a sterile solid phantom made of, e.g., Delrin®. The

performance of the therapeutic light sources may either be monitored by internal and/or external power meters.

Another embodiment of the distributor of the system according to the invention is now described with reference to Figs. 5-8. The distributor 500 comprises two flat and in proximity lying discs made of, e.g. 1 cm thick material such as steel, aluminium/titanium/magnesium, a composite material etc., The lighter the material is, the faster rotation of the discs between fixed positions is possible, while it is important that the discs at the same time are rigid and preferably durable. The discs are hereby arranged on an axis 614, wherein one of the discs is a fixed disc 510 and the other one is a turnable disc 511, wherein the terms "fixed" and "turnable" are merely for the purpose of simplifying the present description. The two discs 510, 511 are rotatable relative each other. In use the discs 510 and 511 are arranged in close proximity against each other, as shown in Fig. 6 and Fig. 8 and for illustrative purposes separated from each other, as shown in Fig. 5 and Fig. 7.

Evenly distributed holes 513 lying on a circle are arranged in both discs (Fig. 7) for fixation of radiation conductors 520, 530, 540. Preferably the diameter of the holes is 0.1 - 0.7 mm. In order to attain a high precision, allowing the light conductors to be arranged exactly face to face, the holes of the two discs can be drilled together, e.g. with a centring tube. Alternatively, high precision cutter or drilling machines may be used for producing the discs or any other mechanical elements mentioned in this description. Then the common axis 614 is utilised arranged at centrally located holes 512 of the

discs 510, 511. It is thus possible to achieve a very high precision when making the series of holes.

By employing discs drilled together, radiation conductors can be fixed in said discs, wherein an extra, thinner disc then can be turned slightly, preferably spring-loaded, so that all light conductors are simultaneously pinched in their positions without the need for any glue or other fixation means. Alternatively, the diameter of the holes is made larger than the diameter of the light conductors, wherein the holes can be dressed with an appropriate piece of tubing, or the ends of the light conductors can be supplied with a fitted hose. Alternatively, the ends of the light conductors can be flared or flanged into the holes or the holes may be equipped with appropriate SMA connector or other type of connectors for receiving radiation conductors. The same principle applies to the holes 2 and fixation of radiation conductors in the translatory radiation distributors as described with reference to the previous embodiments or the current embodiment.

Preferably the radiation conductors are optical fibres, wherein different types of hoses or flexible tubes containing a radiation-conducting material are included. The light conductors should have such a length and be arranged in such a way that the discs can be turned a full turn (+-180 degrees) without problems. The direction of movement may be reversed to avoid the light conductors forming a spiral. The same principle applies to the translatory elements disclosed in this description, wherein the radiation conductors connected to the translatory elements should have such a length that the function of the

translatory elements or the radiation conductors is not negatively influenced. Moreover, the length of the radiation conductors should be sufficiently long, that the positioning of the distal ends of the patient radiation conductors are not negatively influenced.

According to this embodiment of the invention, a plurality of first light conductors 520 in a system for PDD, PDT and PTT are arranged in fixed disc 510 for conduction of radiation to and from a reaction site 801. By a reaction site we in the present context mean a site where photodynamically active compounds will react in a tumour when subject to therapy e.g., by being forwarded through the lumen of injection needles which are placed in the tumour, these radiation conductors 520 are then fixed in the reaction site 801. Then the radiation conductors are moved forward to arrive outside the distal end of the needle. The same light conductor 520 is used continuously during the treatment for integrated diagnostics and dosimetry as well as to avoid that the patient be subjected to multiple pricks.

The holes 513 in the fixed disc as well as in the turnable disc are arranged on a circular line, wherein the circle radius on one disc equals the circle radius on the other disc. The holes on one disc are equally distributed along the circle line with an angular separation of $v_1 = (360/n_1)$ degrees, where n_1 equals the number of holes, and the holes of the other disc are equally distributed along the circle line with an angular separation v_2 equalling $(360/n_2)$ degrees. The first ends of the first radiation conductors 520 are fixed in the holes of the turnable disc 510, and first ends of the second radiation conductors 530,

540 are fixed in the holes of the fixed disc 511. In order to make the holes, and thereby the radiation conductors in both discs connectable to each other in different constellations by turning of the turnable disc 510, n_2 is selected to be a multiple of n_1, in such a way that n_2 is obtained as an integer larger or equal to 1. Suitably the number of holes in the fixed disc is chosen from two to more than six, e.g. two, three, four, five, six, seven, eight, nine or ten.

According to the currently described embodiment, six holes are arranged in the turnable disc 510 and twelve holes are arranged in the fixed disc 511, wherein the terms "fixed" and "turnable" are merely for explanatory reasons in order to simplify the description of the two discs being rotatable relative each other. With six first radiation conductors 520 the angular separation of the holes will accordingly become 60 degrees in the turnable disc 510 and with twelve holes arranged in the fixed disc 511 the angular separation will become 30 degrees for the second radiation conductors 540, 530.

According to the invention, a translatory sliding element 550 is arranged in the fixed disc 511. The sliding element is arranged in disc 511 such that it may be displaced radially outwards on disc 511 by a radially translatory movement, as indicated by the arrow 551. Sliding element 550 receives radiation conductors, similarly as described above with reference to the attachment of fibres in the discs. Element 550 locks in place in such a position that transmission of radiation from one of fibre 563, 564, 565 to a corresponding fibre 520 is as little obstructed as possible, depending on the

currently active light source 560, 561 or 562. In that way it is made possible to couple one radiation conductor at a time (564 in Fig. 5) from a plurality of radiation conductors 563, 564, 565 to a corresponding fibre in the turnable disc 510.

In order to facilitate the comprehension of the invention the following description of a preferred embodiment of the distributor of the system according to the invention relates to six first radiation conductors 520 arranged in the turnable disc 510 for conduction of radiation to and from the reaction site 801.

Thus, the fixed disc 511, as well as the turnable disc 510, have six holes 513 for corresponding second radiation conductors, and, for disc 511, in addition, six further holes for second radiation conductors. All these radiation conductors can release radiation to the reaction site 801 and receive radiation from said site. Thus, several measurements can be recorded and read out simultaneously.

By turning the turnable disc 510 the first and the second radiation conductors become connectable to each other in different constellations. An exact positioning of the opposing radiation conductors in the distributor 500 is facilitated by arranging means for stopping the turnable disc 510 in pre-determined angular positions, for instance, grooves may be arranged in the axis 614 for catching a spring-loaded ball arranged in the turnable disc 510 (not shown in the Figs.) or an angular detector on the rotatable disc can be used. Alternatively electronic regulation using stepmotors or servomotors may be used for this purpose, also in combination with the above described "seventh hole" method.

In order to allow a fast and efficient switching between a diagnostic mode and a therapeutic mode, every second of the second light conductors of the distributor 500 according to the invention, are divided into a first and into a second series. Both series of holes are arranged on the same circle, but displaced by 30 degrees with regard to each other. A specific light conductor in the first series of every other second light conductor is arranged for emitting radiation from at least one radiation source. The other, non specific radiation conductors in the first series of second radiation conductors are arranged for conduction of radiation to at least one radiation sensor 610. The second series of every other second radiation conductor is for therapeutical purposes arranged to emit radiation to the reaction site 801 from at least one radiation source.

The radiation conductors are preferably optical fibres, which in the distributor 500 shown in Figs. 5-8 are connected to the fixed disc 510 as well as the turnable disc 511. Out of the fibres, which are connected to the turnable disc 511, six fibres can be used for diagnostic purposes and six can be used of therapeutical purposes. However, in the diagnostic mode, radiation from one to more than three modalities 560, 561, 562 can be employed.

With reference to Figs. 5-6 only the presently described radiation conductors which are coupled to a turnable disc are for clarifying purposes shown; the other radiation conductors are not shown although they are coupled to said disc, as shown in Figs. 7 and 8.

By turning the turnable disc 510 by 30 degrees the fibres 520 which are optically coupled to the tissue of the patient can be employed for therapy as well as diagnostics and measurements. One out of every second radiation conductor fixed on disc 511 is in the diagnostic mode connected to different radiation sources for diagnostics, while the other five radiation conductors receive signals, which are related to the interaction of these radiation sources with the tissue. Radiation conductors 540 (not all six shown in Fig. 5) are connected to therapeutic radiation sources, e.g. lasers, whereas radiation conductors 530 are connected to radiation detectors. Radiation conductors 563-565 are coupled to diagnostic radiation sources 560-562.

Since intensity as well as spectral resolution is of interest, the distal ends of these five radiation conductors 640 are arranged in a slit-like arrangement so that they overlap the entrance slit and/or constitute the entrance slit of the radiation sensor 610, which may be a compact spectrometer or other type of detector and is supplied with a two-dimensional detector array or one to several one dimensional detector arrays. The recording range of the spectrometer is preferably within the range 400 to 900 nm. Each of the radiation conductors 530 can of course be connected to an individual radiation detector 610 in the form of a spectrometer or another type of detector, e.g. a compact integrated spectrometer.

With reference to Fig. 6, the assembly 600 is shown with the two discs 510, 511 on a common axle 614 and the translatory element 550 for switching between different diagnostic light sources is integrated in disc 511. In this way a more compact and robust construction is obtained

compared to other solutions having an external radiation distributor for switching between the diagnostic light sources.

Preferably one of the radiation sources 560, 561, 562 is a laser of the same wavelength as the ones utilised for the laser irradiation for photodynamic tumour therapy, but could be of lower output power. Suitable filters can be arranged on radiation distributor 550, to be moved into the light path of the radiation sensor 610 in order to secure that the correct dynamic range is utilised for all measurement tasks.

Certain of the radiation sources 560, 561, 562 are utilised in order to study how radiation (light) of the corresponding wavelength is penetrating through the tissue of the tumour. When light from a radiation source is transmitted through the particular radiation conductor via radiation distributor 550 and the discs 511, 510 into the tissue, one of the first radiation conductors 520, which is the one opposing the radiation conductor in the distributor 550, will function as a transmitter in the tumour, and the other five radiation conductors 520 in the tumour will act as receivers and collect the diffuse flux of light reaching them. The light collected is again conducted via the discs 510, 511 and via radiation conductors 640 (whereof two conductors are shown in Fig. 5 at 530) to the radiation sensor 610 and five different light intensities can be recorded on the detector/detectors/detector array.

When the turnable disc 510 is turned by 60 degrees, the next radiation conductor 520 to the patient will get the role as transmitter, and the five others become the receivers for a new light distribution. After four further

turns of the turnable disc 510, each by 60 degrees to the following radiation conductor 520 in the patient, light flux data for all remaining combinations of transmitters/receivers have been recorded. Thus, in total 6 x 5 = 30 measurement values are obtained and can be used as input data for a tomographic modelling of the optical dose build up in the different parts of the tumour during the course of the treatment. Furthermore, by switching through the three light sources 560-562, by means of translatory moving radiation distributor 550, these 30 measurement values are multiplied by the number of radiation sources, resulting in 90 tomographic measurement values.

In addition to a specific wavelength, radiation from a white light source and/or broadband light emitting diodes and/or line light sources can be coupled into the particular active light conductor in radiation distributor 550. On passage through the tissue to the receiving light conductor 520 in the patient, the well-defined spectral distribution of the radiation source will be modified by the tissue absorption. Then, oxygenated blood yields a different signature than non oxygenated blood, allowing a tomographic determination of the oxygen distribution utilising the thirty different spectral distributions which are read out, five spectra at a time in the six possible different constellations on rotation of the turnable disc 510 during a diagnostic investigation. Such a determination of the oxygenation in the tumour is important, since the PDT process requires access to oxygen in the tissue.

Finally, a light source for blue/violet or ultraviolet light, e.g. a laser, can be coupled to the particular active radiation conductor in radiation distributor 550.

Then fluorescence is induced in the tissue, and a sensitizer administered to the tissue displays a characteristic red fluorescence distribution in the red/near-infrared spectral region. The strength of the corresponding signal allows a quantification of the sensitizer level in the tissue.

Since the short wavelength light has a very low penetration into the tissue, the induced fluorescence will only be measured locally at the tip of the radiation conductor. For this task there is in this case for the corresponding radiation source 670 at the distal end of the particular radiation conductor 661 a beamsplitter 660, connected via the radiation conductor 662 and which is preferably a dichroic beamsplitter, transmitting the exciting light but reflecting the red-shifted fluorescence light. This reflected light is focused into the distal end of a conveying radiation conductor 662, the other end of which is connected to the radiation sensor 610, which records the fluorescence light distribution. A suitable self-contained fluorosensor is described in Rev. Sci. Instr. **71**, 510004 (2000). Such a system with dichroic beamsplitters may also in a similar way be implemented by means of the translatory radiation distributor system as shown in Figs. 1-4. For instance radiation conductor 662 may be inserted between radiation detector 130 and a dichroic beamsplitter 660 being inserted in e.g. radiation conductor 144.

By rotating the turnable disc 510, the fluorescence that is proportional to the concentration of the sensitiser, can be measured sequentially at the tips of the six radiation conductors. Since the sensitizer is bleached by the strong red treatment light, being particularly strong

just around the tip of the radiation conductor 520 conducting radiation to the patient, it is essential to make this measurement before the start of the treatment.

If the tips of the radiation conductors 520, 120a-120f in addition are treated with a material, the fluorescence properties of which are temperature dependent, sharp fluorescence lines are obtained upon excitation, and the intensity of the lines and their relative strength depend on the temperature of the tip of the radiation conductor 520,120a-120f being employed for treatment. Examples of such materials are salts of the transition metals or the rare earth metals. Thus also the temperature can be measured at the six positions of the six radiation conductors, one at a time. The measured temperatures can be utilised to find out if blood coagulation with an associated light attenuation has occurred at the tip of the radiation conductor 520,120a-120f and for studies regarding the utilisation of possible synergy effects between PDT and thermal interaction. Since the lines obtained are sharp, they can be lifted off the more broad-banded fluorescence distribution from the tissue.

The concentration of the sensitizer can for certain substances be measured in an alternative way. Then the red light used for the light propagation studies is used to induce near-infrared fluorescence. This fluorescence penetrates through the tissue to the tips of the receiving radiation conductors 520,120a-120f, and are displayed simultaneously as spectra obtained in the radiation sensor 610, 130. A tomographic calculation of the concentration distribution can be performed based on in total thirty measurement values.

After diagnostic measurements and calculations have been performed, the fibres 520 optically coupled to the tissue of the patients can be utilised for therapy by rotation of the turnable disc 510 by 30 degrees. Therapeutic radiation sources are thus coupled to the patient fibres 520. The therapeutic radiation sources are preferably laser sources with a wavelength, which is adapted to the absorption band of the sensitizer. At the photodynamic tumour treatment a dye laser or a diode laser is preferably used, with a wavelength which is selected with regard to the sensitizer employed. For Photofrin® the wavelength is 630 nm, for δ-aminolevulinic acid (ALA) it is 635 nm and for phthalocyanines it is around 670 nm. The individual lasers are regulated during the treatment to a desirable individual output power. If desired, they may have built-in or external monitoring detectors.

The therapeutical treatment can be interrupted and new diagnostic data can be processed in an interactive method until an optimal treatment has been reached. This method can include synergy between PDT and hyperthermia, where an increased temperature is reached at increased fluxes of laser radiation. The whole process is controlled using a computer, which does not only perform all the calculations but also is utilised for regulation.

The radiation distributors described are preferably driven by stepper motors / servomotors in order to move between the different constellations.

The present invention has been described above with reference to specific embodiments. However, other embodiments than the preferred above are equally possible within the scope of the appended claims, e.g. different

shapes of the translatory elements than those described above, performing the above method by hardware or software, etc.

Furthermore, the term "comprises/comprising" when used in this specification does not exclude other elements or steps, the terms "a" and "an" do not exclude a plurality and a single processor or other units may fulfil the functions of several of the units or circuits recited in the claims.

CLAIMS

1. A system for therapy and/or diagnosis of a mammal comprising at least one first radiation source for emission of a diagnostic radiation, and at least one first radiation conductor adapted to conduct radiation to a site at or in said mammal, **characterised** by at least one distributor for distribution of said diagnostic radiation from at least the first radiation source to the treatment site, wherein the distributor comprises at least one translatory element being arranged in such a manner that radiation is coupled in different constellations by translatory movement of said translatory element between pre-determined positions.

2. The system according to claim 1, said therapy and/or diagnosis being tumour therapy and diagnosis, said treatment site being a tumour site.

3. The system according to claim 2, comprising at least one second radiation source for emission of a therapeutic radiation through at least one of said radiation conductors to said site.

4. The system according to claim 2 or 3, said tumour therapy and diagnosis being interactive interstitial photodynamic tumour therapy and/or photothermal tumour therapy and/or tumour diagnosis.

5. The system according to any of claims 2 to 4, wherein the radiation conductor is in use employed as a

transmitter and/or a receiver for conduction of radiation to and/or from the tumour site for diagnosis and/or therapy of a tumour at the tumour site, **characterised** by

a plurality of first radiation conductors arranged for conducting radiation to and from the tumour site,

a plurality of second radiation conductors arranged for delivering radiation from at least one radiation source and/or conduction of radiation to at least one radiation sensor, and

wherein said distributor is a distributor for distribution of radiation from at least one radiation source to the tumour site and/or from the tumour site to at least one radiation sensor, wherein the distributor comprises at least one translatory element being arranged in such a manner that radiation is coupled in different constellations by translatory movement of said element between pre-determined positions relative to another element.

6. The system according to claim 5, **characterised** in that each element has holes arranged for receiving said radiation conductors and that corresponding holes on the two elements are equidistantly arranged on a straight line.

7. The system according to claims 5 or 6, **characterised** in that first ends of the first radiation conductors are fixed in the holes of a translatory displacement element and first ends of second radiation conductors are fixed in the holes in the other element, wherein the first and the second radiation conductors are

connectable to each other in different constellations through said translatory movement between pre-determined positions of the translatory displacement element and the other element relative each other.

8. The system according to claim 7, **characterised** in that said other element is a second translatory displacement element.

9. The system according to claim 6, **characterised** by two flat discs in close proximity to each other, wherein said discs are turnable relatively to each other,

each disc having holes arranged on a circular line, wherein the circle radius on one disc equals the circle radius on the other disc and where the holes in one disc are equally distributed on the circle line with an angular separation of $v_1=(360/n_1)$ degrees, n_1 being the number of holes, and the holes in the other disc are equally distributed on the circle line with an angular separation of $v_2=(360/n_2)$ degrees, wherein $n_2 = m \times n_1$, and wherein m is a multiple, which yields n_2 as an integer ≥ 1, and

wherein the first ends of the first radiation conductors are fixed in the holes of the first disc and first ends of the other radiation conductors are fixed in the holes of the second disc, whereby the first and the second radiation conductors by rotation of the turnable disc are connectable to each other in different constellations, and wherein said other element is one of said discs, wherein the translatory element is comprised in said other disc to couple between a plurality of third

radiation conductors to one of said first radiation conductors and by replacing one of said second radiation conductors.

10. The system according to claim 9, **characterised** by n_1 being the number of holes in the second disc of the distributor, $n_1 = 6$ and $m = 2$, yielding $n_2 = 12$ holes in the first disc of the distributor.

11. The system according to claim 9 or 10, **characterised** by every other second radiation conductor being part of a first series of second radiation conductors and that a radiation conductor in said first series of second radiation conductors being arranged for emitting radiation from the radiation source and the other radiation conductors in said first series of second radiation conductors being arranged for conduction of radiation to the radiation sensor.

12. The system according to any of claims 9 to 11, **characterised** in said translatory element is arranged radially displaceable in said other disc, said third radiation conductors being connected to diagnostic radiation sources, such that the translatory element in said other disc couples one of said diagnostic radiation sources to one of said first radiation conductors in said first disc.

13. The system according to any of claims 1 to 12, **characterised** by the diagnostic radiation source being

a light source for near-infrared (NIR), white, red, blue/violet and/or ultraviolet light.

14. The system according to any of claims 1 to 13, **characterised** by the diagnostic radiation source comprising a beamsplitter.

15. The system according to claim 14, **characterised** by a transferring radiation conductor being arranged between a dichroic beamsplitter and the radiation sensor.

16. The system according to claim 13, **characterised** by the first radiation conductors second ends being treated by a material with temperature sensitive fluorescence emission.

17. The system according to claims 9 or 10, **characterised** by every second other radiation conductor being part of a second series of second radiation conductors arranged for emission of radiation from the radiation source.

18. The system according to claims 3 to 17, **characterised** by the therapeutic radiation source being a light source for coherent light of a single fixed wavelength.

19. A system according to any of claims 1 to 18, **characterised** by the distributor including means for

locking the radiation distributor into pre-determined transversal and/or azimutal positions.

20. A system according to any of the preceding claims, **characterised** by the radiation conductors being optical fibres.

21. The system according to claims 13 to 15, **characterised** by fluorescence being recorded through the same radiation conductor as the one transmitting radiation to the tumour site.

22. The system according to claim 16, **characterised** in that for interactive photodynamic therapy one or several of the radiation conductors which are treated with the material with a temperature sensitive fluorescence emission are measuring the temperature at the tumour site,

that the radiation which is sent to the tumour site heats the tumour site,

that the intensity of the radiation is controlled by the measured temperature in order to regulate the temperature of the tumour site at the individual radiation conductors.

23. The system according to any of the preceding claims, **characterised** in that said translatory displacement element is an optical sledge.

24. The system according to any of the preceding claims, **characterised** by at least one stepping motor or at

least one servo system for moving said elements of said radiation distributor relative each other.

25. The system according to any of the preceding claims, **characterised** in that said constellations are modes of the system from the list of: interactive interstitial photodynamic tumour therapy, photothermal tumour therapy using hyperthermia, and tumour diagnostics, whereby these modes are alternatively used during the same occasion of treatment of said tumour site.

26. The system according to any of claims 3 to 25, **characterised** by said system comprising

a diagnostic mode, wherein one diagnostic radiation source being coupled via a first translatory element to said first radiation conductors transmitting diagnostic light to said site and the remaining first radiation conductors being coupled to a radiation detector, and

a therapeutic mode, wherein said therapeutic radiation sources are coupled to said first radiation conductors transmitting therapeutic radiation to said site.

27. The system according to claim 26, **characterised** in that at least one second translatory element switches between the modes.

28. The system according to claim 27, **characterised** in that a third translatory element switches between a plurality of radiation conductors from said second translatory element to said radiation detector.

29. A method for interactive interstitial photodynamic tumour therapy and/or photothermal tumour therapy and/or tumour diagnosis, wherein at least one radiation sensor and radiation conductor is connected to a tumour site and the radiation conductor is used as a transmitter and/or a receiver for conduction of radiation to and/or from a tumour site for diagnosis and therapy of a tumour at the tumour site,

characterised in that the switching between tumour therapy and tumour diagnostics is achieved in an automatised way by switching radiation conductors between different constellations by means of a radiation distibutor comprised in the system according to claim 1, and

that the results from the diagnostics control the therapy process by regulating a therapeutical radiation intensity depending on the results of the diagnostics until an optimal treatment of the tumour site has been achieved.

30. The method according to claim 29, **characterised** by alternatingly utilising interactive interstitial photodynamic tumour therapy, photothermal tumour therapy using hyperthermia, and tumour diagnostics during the same occasion of treatment of said tumour site.

ABSTRACT

A system and method for interactive interstitial photo-dynamic tumour therapy and/or photothermal tumour therapy, said system comprising at least one distributor, which is arranged for distribution of radiation from at least one radiation source to a reaction site, or from the reaction site to at least one radiation sensor, wherein a plurality of first radiation conductors are arranged for conduction of radiation to and from the reaction site and a plurality of second radiation conductors are arranged for emitting radiation from the radiation source and/or conduction of radiation to the radiation sensor, where the reaction site is a tumour. The radiation distributor comprises at least one translatory displacement element being translatory movable relatively to another element. Each element has holes arranged for receiving said radiation conductors, such that corresponding holes on the two elements are equidistant arranged on a straight line. The first ends of the first radiation conductors are fixed in the holes of the first translatory displacement element and first ends of the second radiation conductors are fixed in the holes in the other element, wherein the first and the second radiation conductors are connectable to each other in different constellations through translatory movement of the translatory displacement element and the other element relative each other.

To be published with Fig. 4

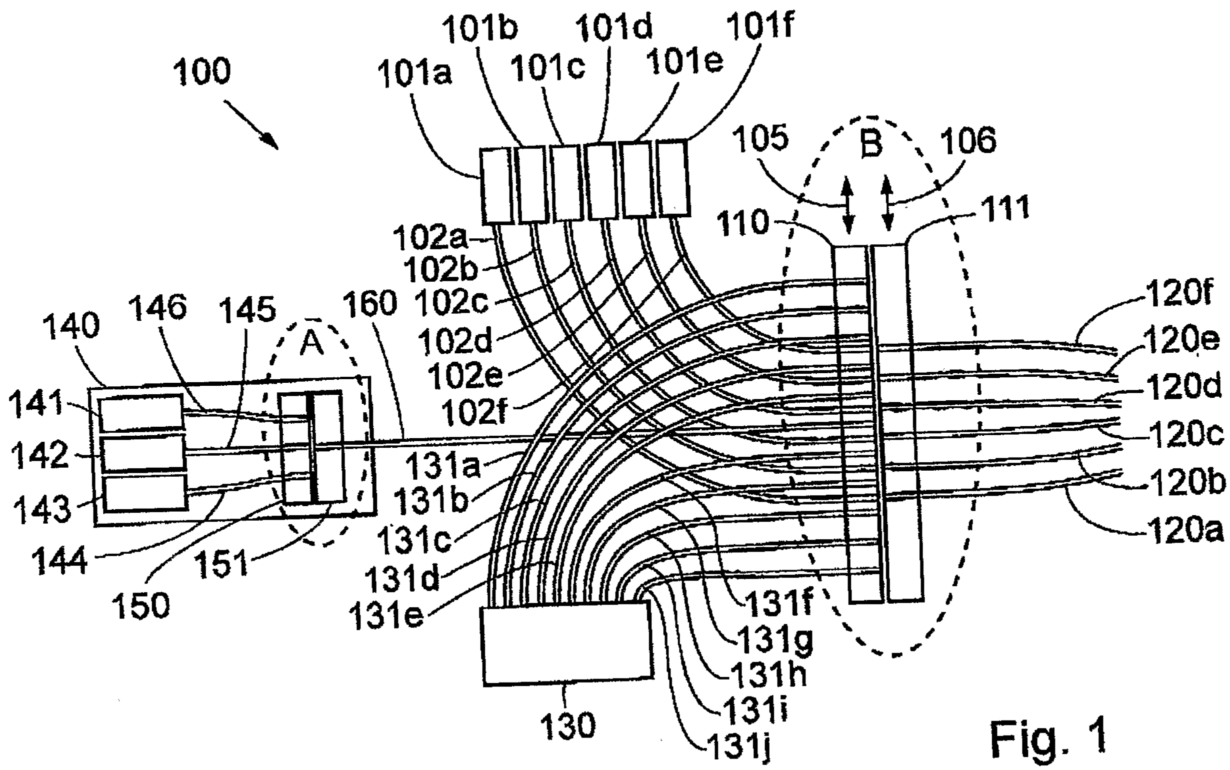
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Fig. 1

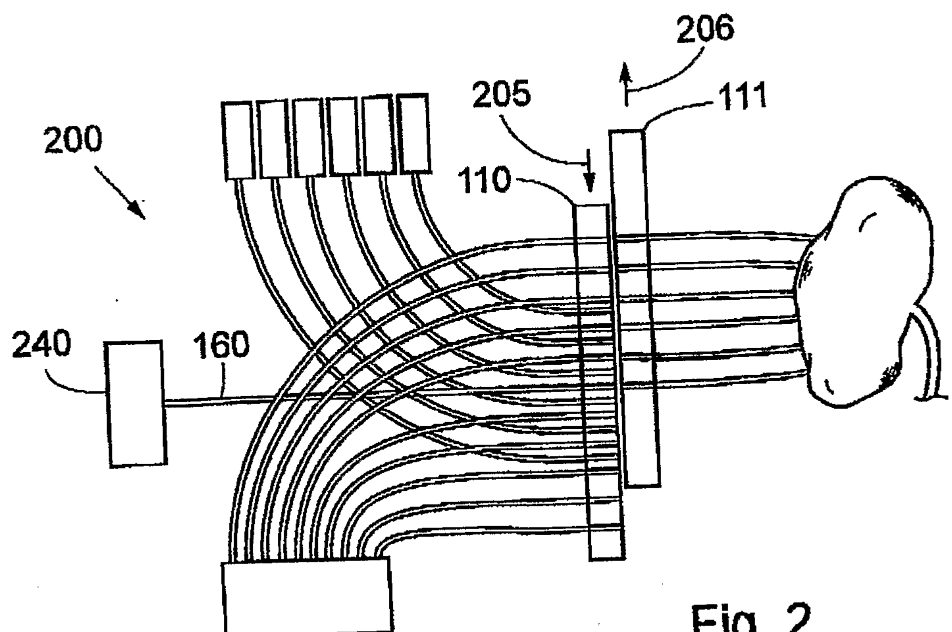
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Fig. 2

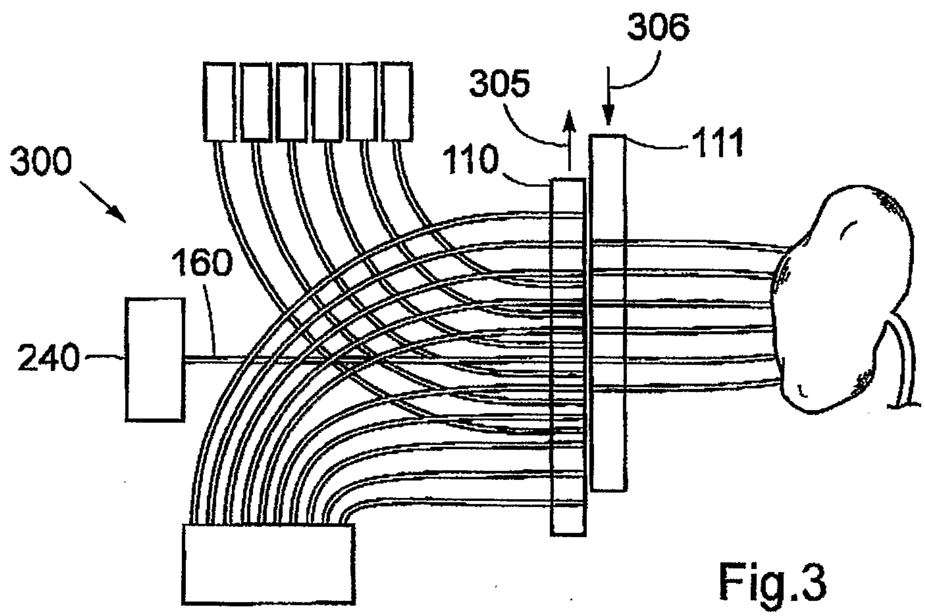
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Fig.3

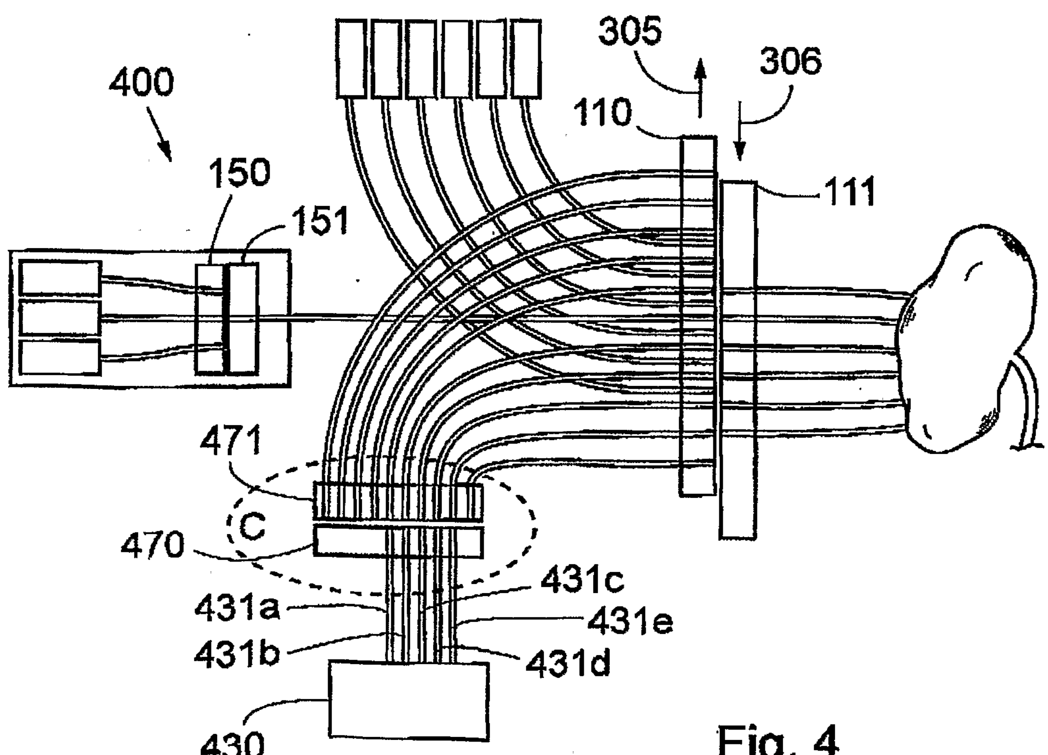
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Fig. 4

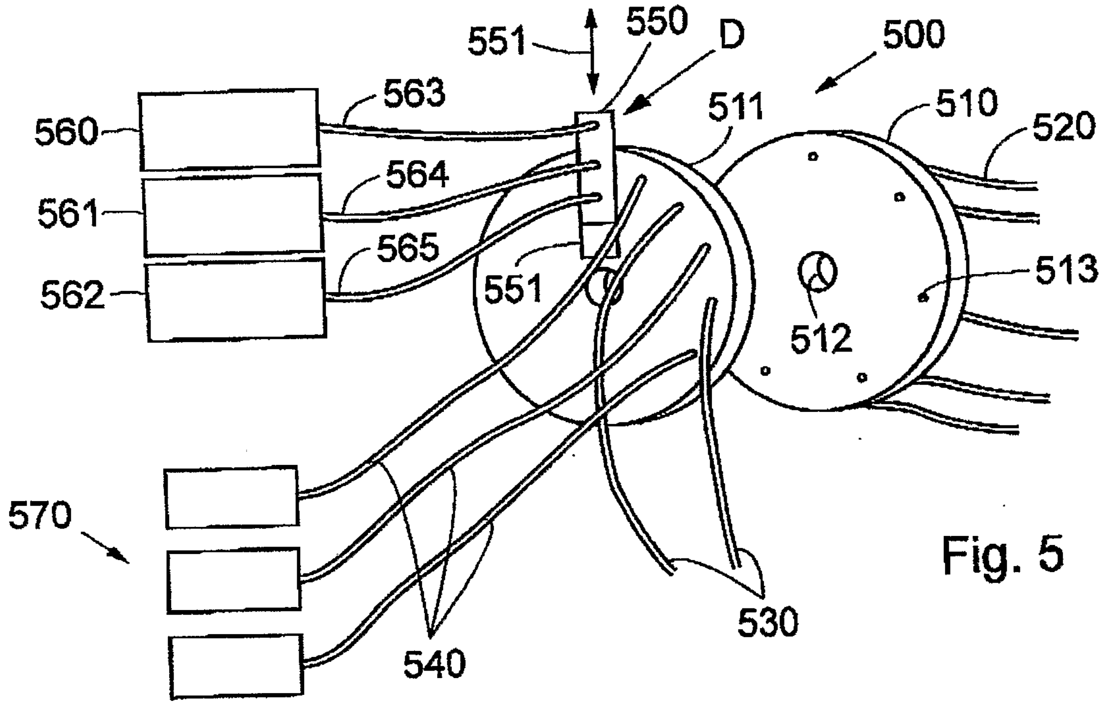
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Fig. 5

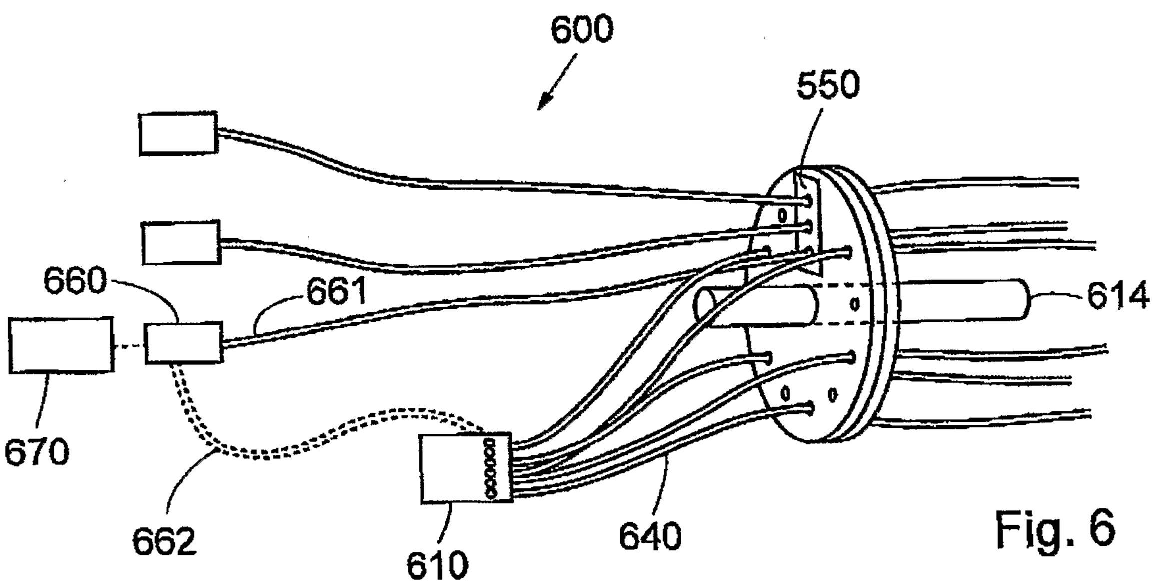
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Fig. 6

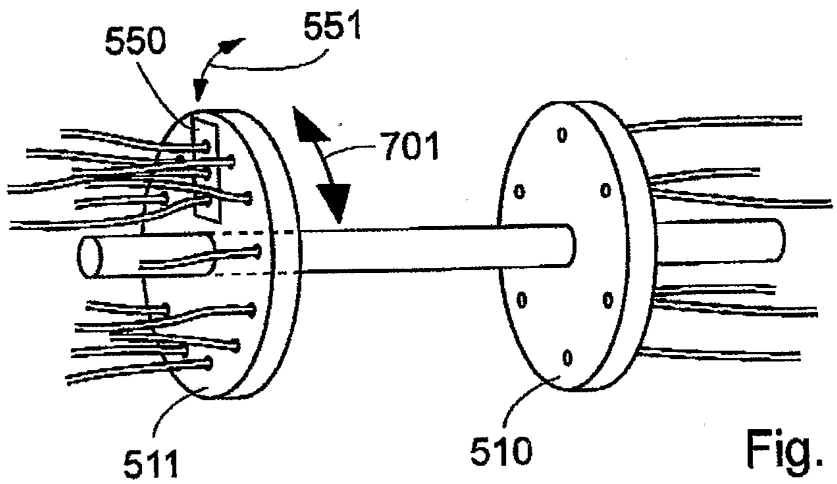

Fig. 7

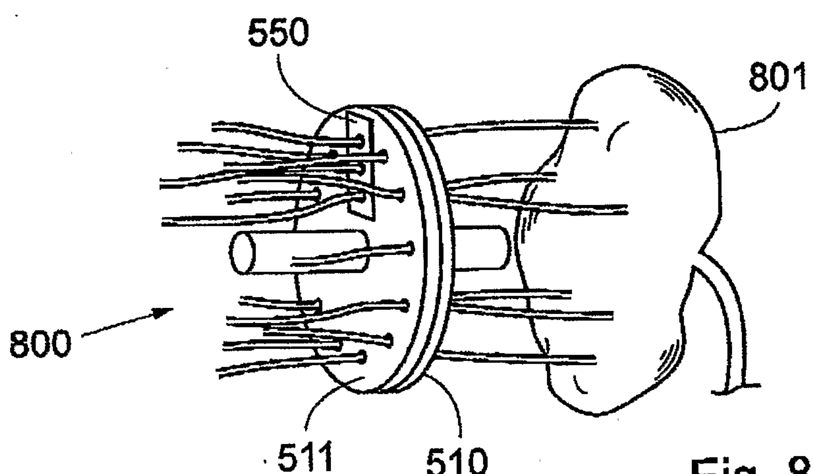

Fig. 8

Fig. 9